

EVIDENCE ON DEVELOPMENTAL AND REPRODUCTIVE TOXICITY OF SODIUM NITRITE

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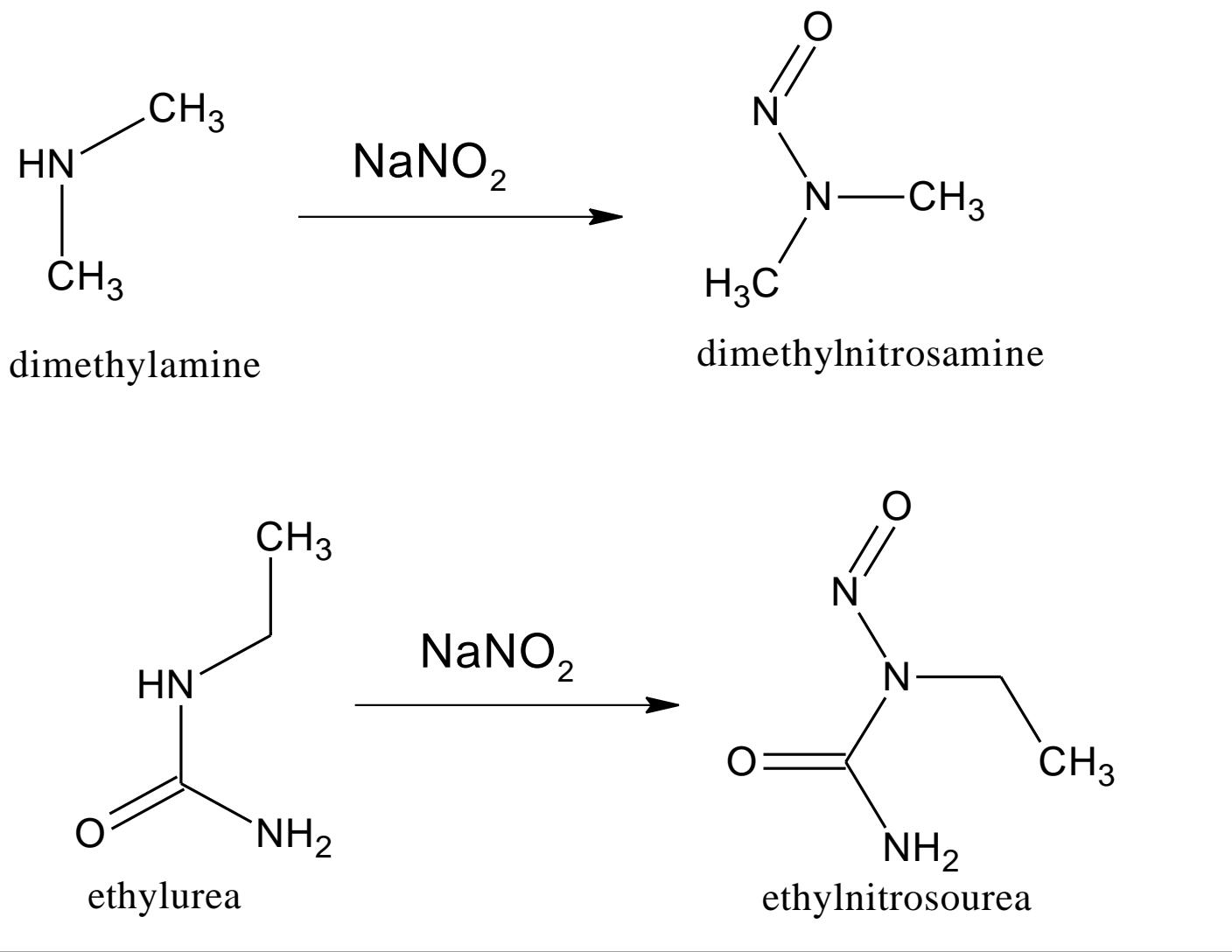


Transplacental carcinogenesis

- Animal studies and other relevant data
- Epidemiologic studies



Formation of N-nitroso Compounds



Sources of

- endogenous production
 - e.g., histamine, spermine, tyramine
- foods
 - e.g., meats, fruits, vegetables, grains
- beverages
 - e.g., wine, beer, coffee, tea
- medicines
 - e.g., antihistamines, antibiotics, tranquilizers



Inhibitors of nitroso f

- Vitamin C (ascorbic acid)
- Polyphenols
- Other antioxidants (e.g., vitamin E)



Endogenous production of vitamin C

Human	No
Guinea pig	No
Hamster	Yes
Rat	Yes
Mouse	Yes



Other Relevant Data: Cancer studies of N-nitroso compounds

- Nitrosamines
 - tumors of the liver, esophagus, nasal and oral mucosa, kidney, pancreas, bladder, lung, thyroid
- Nitrosoureas
 - tumors of lymphatic and nervous system



Other Relevant Data: Transplacental cancer studies of N-nitroso compounds

- Nitrosoureas
 - brain, spinal cord, PNS tumors in the rat
 - hematopoietic tumors in the mouse
 - kidney, liver, lung tumors in the hamster



Animal studies of transplacental carcinogenesis

Species	NaNO ₂ alone	NaNO ₂ + amine/amide
Hamster	2	3: ethylurea (2), morpholine
Rat	3	3: L-citrulline, morpholine, diethylamine
Mouse	2	1: cimetidine

Prenatal exposure

Hamster (gd 15)	NaNO ₂ alone +ethylurea	---- PNS tumors (*inhibited by ascorbate)	Rustia, 1975
Hamster (gd 12- 15)	NaNO ₂ + ethylurea	PNS tumors	Rustia & Schenken, 1976
Rat (gd 13- 23)	NaNO ₂ alone + citrulline	---- Wilms' tumor (kidney)	Ivankovic, 1979



Pre- & postnatal exposure

Hamster	NaNO ₂ alone + morpholine	---	Shank & Newberne, 1976
Rat	NaNO ₂ alone + morpholine	Lymphoreticular, total tumors (other than liver & angiosarcomas) Liver carcinoma, Angiosarcoma of Liver, Lung	Shank & Newberne, 1976
Rat	NaNO ₂ alone +diethylamine	---	Druckery <i>et al.</i> , 1963
Mouse	NaNO ₂ alone + cimetidine	Lung, Lymphoma Lung	Anderson <i>et al.</i> , 1985
Mouse	NaNO ₂ alone	---	Hawkes <i>et</i> <i>al.</i> , 1992

